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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
03/31/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,412	SAKURAGAWA ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/22/05, 12/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Human bone stem cells from amniotic mesenchymal cell layer.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-5 disclose the limitation of "bone stem cells existing in human amniotic mesenchymal cell layer". It is not clear what this limitation intends to claim. It can be interpreted that bone stem cells isolated from human amniotic mesenchymal cell layer or bone stem cells as being physically present in the human amniotic mesenchymal cell layer without isolation. In other words, it is vague whether the limitation points out isolated bone stem cells or the mesenchymal cell layer containing bone stem cells.

Clarification is required.

Claim 5 provides for the use of a bone stem cell for osteogenesis, however, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 2 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed invention does not fall within at least one of the four categories of patent eligible subject matter recited in 35 U.S.C. 101 (process, machine, manufacture, or composition of matter). The current claim is drawn to cells in human amniotic mesenchymal cell layer, without any step of process (e.g. isolation, purification). Thus, the claimed subject matter is not considered as a man-made product, instead it is drawn to a product of the nature. The standard for patentability in the area of living organisms and biomolecules is whether the claimed matter "is the result of human intervention." See M.P.E.P. § 2105.

Claim 5 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35

U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Hung et al. (US 2002/0045260) in light of Whittle et al. (2000; Placenta).

Claims are drawn to a bone stem cell separated from human amniotic mesenchymal cell layer; cells for forming bone cells comprising bone stem cells in human amniotic mesenchymal cell layer; a method for obtaining bone cells by culturing bone stem cells in a bone cell-differentiation medium; a method of transplanting bone stem cells from human amniotic mesenchymal cell layers into bone defects.

Hung et al. teach mesenchymal stem cells capable of differentiating into bone cells (see abstract) obtainable from placenta (see para. 26), and a method of culturing mesenchymal stem cells in an osteogenic culture medium to differentiate the mesenchymal stem cells into osteoblasts (see para. 37, Example 4). Hung et al. also teach a method of tissue replacement (considered as transplantation) using mesenchymal stem cells (see abstract), and transplanting mesenchymal stem cells (see para. 32).

Claim 1 is a product-by-process claim. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product

claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Nevertheless, Hung et al. disclose the source of human mesenchymal stem cells being placenta (see above) and it is well known in the art that amniotic mesenchymal cell layers is a part of amniotic membrane of placenta in light of Whittle et al. (see abstract and p.395), the mesenchymal stem cells of the references derived from placenta are considered to encompass the mesenchymal stem cells separated from amniotic mesenchymal cell layer.

Thus, the reference anticipates the claimed subject matter.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Whittle et al. (supra) in light of Nikaido (WO/2003/047607; IDS reference) and Alviano et al. (2007, BMC Dev. Biol.).

Claim 2 is drawn to cells comprising bone stem cells from human amniotic mesenchymal cell layer.

Whittle et al. teach human amniotic mesenchymal cells (see whole document).

Although Whittle et al. do not particularly teach the mesenchymal cells comprise a bone stem cell, it is an inherent property of human amniotic mesenchymal cells of Whittle et al. to contain mesenchymal stem cells which can differentiate into bone cells (thus osteogenic stem cells) as evidenced by Nikaido. Nikaido teaches mesenchymal

cells from amnion have capability to regenerate and are suitable for replacing the human fetal stem cells, and usable as a remedy for bone metabolic errors (see abstract). Furthermore, Alviano et al. provide evidence that amniotic membrane is a high throughput source for multipotent mesenchymal stem cells (see abstract). Therefore, it is clearly an inherent property of mesenchymal cells isolated from human amniotic membrane of Whittle et al. to comprise multipotent mesenchymal stem cells.

M.P.E.P. §2112 states that "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. *v.* Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re* Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In *In re* Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel."

Therefore, a holding of anticipation is clearly required.

Claims 1, 2 and 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Nikaido (supra) in light of Alviado et al. (supra).

Claims are drawn to a bone stem cell separated from human amniotic mesenchymal cell layer, and use of the bone stem cells for osteogenesis.

Nikaido teaches mesenchymal cells originated from human amnion (thus they are from amniotic mesenchymal cell layer), and these cells are usable as a substitute for human fetal stem cells because of their regenerative ability, and used as a remedy for bone metabolic errors (see abstract).

Although Nikaido does not particularly disclose the mesenchymal cells being "bone stem cells", based on the evidence of Alviado et al. that amniotic membrane is a source for a significant amount of mesenchymal stem cells, and the teaching of Nikaido that the mesenchymal cells have regenerative ability to replace fetal stem cells, the examiner takes the position that the mesenchymal cells of Nikaido contain mesenchymal stem cells.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' bone stem cells differ, and if so to what extent, from the mesenchymal cells discussed in Nikaido. Accordingly, it has been established that the prior art mesenchymal cells, which has the same property of being able to regenerate and to be used for bone defect, demonstrates a reasonable probability that it is either identical or sufficiently similar to the claimed bone stem cells that whatever differences exist are not patentably significant. Therefore, the burden of establishing novelty or unobviousness by objective evidence is shifted to applicants.

Merely because a characteristic of a known product (i.e. mesenchymal cells) is not disclosed in a reference does not make the known cells patentable. The new

product possesses inherent characteristics which might not be displayed in the tests used the reference. Clear evidence that the amniotic mesenchymal cells of the cited prior art do not possess a critical characteristic that is possessed by the claimed bone stem cells, would advance prosecution and might permit allowance of claims to applicants' bone stem cells.

Thus, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hung et al. (supra) in view of Nikaido (supra) or Whittle et al. (supra).

Claims are drawn to a bone stem cell separated from human amniotic

mesenchymal cell layer; a method for obtaining bone cells comprising culturing bone stem cells in human amniotic mesenchymal cell layer in a bone cell-differentiation medium; a method of transplanting bone stem cells to bone defect.

Hung et al. teach mesenchymal stem cells capable of differentiating into bone cells (osteoblasts) derived from placenta (see para. 26), and a method of culturing mesenchymal stem cells in osteogenic culture medium to differentiate the mesenchymal stem cells into osteoblasts (see para. 37, Example 4). Furthermore, Hung et al. teach a method of tissue replacement (considered as transplantation) using mesenchymal stem cells (see abstract), and transplanting mesenchymal stem cells (see para. 32).

Hung et al. do not teach mesenchymal stem cells from amniotic mesenchymal cell layer.

Nikaido teaches mesenchymal cells from amniotic membrane having regenerative capability and being used as a remedy for bone metabolic errors (see abstract). Since it is well known that mesenchymal cells from amniotic membrane are derived from mesenchymal cell layer, the mesenchymal cells of Nikaido are considered to be derived from mesenchymal cell layer.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the mesenchymal stem cells of Hung et al. with amniotic mesenchymal cells of Nikaido et al. in the method of in vitro differentiation of mesenchymal stem cells into osteoblasts, and a method of transplanting mesenchymal stem cells of Hung et al.

The skilled artisan would have been motivated to make such a modification

because a person of ordinary skill in the art recognizes the mesenchymal cells of Nikaido as an art-acceptable equivalent because the mesenchymal cells of Nikaido possess the same property of regeneration as mesenchymal stem cells of Hung et al. and can be used for the same intended use (remedy for bone defect). Therefore, it would have been obvious to a person of ordinary skill in the art to make such substitution of equivalent or alternative in the method of Hung et al. with reasonable expectation of success.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in

substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

In addition, it would have been obvious to a person of ordinary skill in the art to recognize that the mesenchymal stem cells derived from placenta are from amniotic mesenchymal cell layers. This is because it is also well known in the art that placenta comprises amnion (amniotic membrane), and the amniotic membrane is composed of a single layer of epithelial cells, layers of mesenchymal cells according to Whittle et al. (see abstract and Methods and Material, p.395). Therefore, a person of ordinary skill in the art would recognize that the mesenchymal stem cells isolated from placenta as taught by Hung et al. are existing in and derived from mesenchymal cell layers of the human amniotic membrane.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 9:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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